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85. A vector comprising:
- a) a nucleic acid molecule as set forth in any one of claims 61-84; and
 - b) one or more suitable regulatory sequences which induce expression and/or integration of the DNA sequence in a host cell.
86. A host cell transformed with the vector of claim 85. --

REMARKS

The Office Action dated March 16, 2000 has been carefully reviewed and the forgoing amendments are made in response thereto. In view of these amendments and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Applicants respectfully submit that no prohibited new matter has been introduced by the amendments. While written description support for the amended claims can be found throughout the specification, specific support for nucleotide changes in exons 15 and 16, for example, can be found in Figures 1 and 2 and SEQ ID NO: 2 and 3, respectively of the Sequence Listing. Support for the specific polymorphic sites 1093, 1342, 1593, 2457, 2908, 3199, 3624, 4035, 7470 and 9079, including the corresponding amino acid positions, for example, can be found throughout the specification, in Figure 3, and SEQ ID NO: 4-13 of the Sequence Listing.

I. Summary of the Office Action

1. Upon entry of the foregoing amendment, claims 61-86 will be pending.
2. The Office Action requested that the Brief Description of the Drawings be amended to reference the listed nucleotide sequences by SEQ ID NO.
3. The Office Action objected to the drawings.
4. Claims 1-16, 22, 24, 26, 28, 30, and 38 were rejected under 35 U.S.C. § 101 as being drawn to nonstatutory subject matter.
5. Claims 1-16, 22, 24, 26, 28, 30, 38 and 52-54 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for lacking improper antecedent basis, not identifying

specific reference sequences for the claimed nucleotide sequences, and other claim language that renders the claims indefinite.

6. Claims 1-16, 22, 24, 26, 28, 30, 38 and 52-54 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which lacks proper written description.

7. Claims 1 and 9 were rejected under 35 U.S.C § 102(b)/103(a) as being anticipated by, or alternatively, obvious over Futreal et al. (GB 2 307 477, May 28, 1997).

8. Claims 1 and 9 were rejected under 35 U.S.C § 102(b) as being anticipated by, or alternatively, obvious over Tavtigian et al. (Nature Genetics (March 1996)).

9. No claims were allowed.

II. Response to the Office Action

1. Amendment of the Brief Description of the Drawings.

The Office Action objected to the specification because the sequences disclosed in Figures 1 and 2 do not comply with the Sequence Rules under 37 C.F.R. 1.821(d). Applicants have amended the specification to include the requested sequence identifiers (SEQ ID NO), and a corrected paper copy and computer readable form of the Sequence Listing will follow. Applicants respectfully request the objections to the specification be withdrawn.

2. Objections to the drawings.

The drawings were objected to because the figures had multiple panels which were not designated with letters.

Applicant's respectfully request that the objection to the drawings be held in abeyance with the understanding that the corrections suggested in the Office Action will be addressed in the preparation of the formal drawings following notification of allowable subject matter.

3. Rejection of the claims under 35 U.S.C. § 101.

The Office Action rejected claims 1-16, 22, 24, 26, 28, 30, and 38, under 35 U.S.C. § 101, as being drawn to nonstatutory subject matter.

Respectfully, the newly added claims have been written to claim an "isolated nucleic acid molecule." Applicants respectfully request that this rejection of the claims be withdrawn.

4. Rejection of the claims under 35 U.S.C. § 112, second paragraph.

The Office Action rejected claims 1-16, 22, 24, 26, 28, 30, 38 and 52-54, under 35 U.S.C. § 112, second paragraph, as being indefinite for lacking improper antecedent basis, not identifying specific reference sequences for the claimed nucleotide sequences, and other claim language that renders the claims indefinite.

Respectfully, Applicants have canceled claims 1-16, 22, 24, 26, 28, 30, 38 and 52-54 and replaced those claims with new claims 61-86. Furthermore, the substitute claims do not use the terms and phrases "coding sequence," "the coding sequence nucleotides are as follows," "haplotype," "BRCA^(omi#)," "codon pairs," "a BRCA2 coding sequence," "any fragments thereof," or "to induce replication and/or integration in a host cell". Applicants thank the Examiner for her helpful suggestions, which have been incorporated where appropriate and possible. Applicants respectfully request that this rejection of the claims be withdrawn.

5. Rejection of the claims under 35 U.S.C. § 112, first paragraph, as containing subject matter which lacks proper written description.

The Examiner rejected claims 1-16, 22, 24, 26, 28, 30, 38 and 52-54, under 35 U.S.C. § 112, first paragraph, as containing subject matter which lacks proper written description.

Respectfully, for the sole purpose of furthering prosecution, Applicants have canceled claims 1-16, 22, 24, 26, 28, 30, 38 and 52-54 without prejudice and replaced those claims with new claims 61-87, the support for which can be found in the specification as described herein.

Applicants respectfully request that this rejection of the claims be withdrawn.

6. Rejection of the claims under 35 U.S.C § 102(b)/103(a).

The Office Action rejected claims 1 and 9 under 35 U.S.C § 102(b)/103(a) as being separately anticipated by Futreal *et al.* (GB 2 307 477, May 28, 1997) and Tavgian *et al.*, or alternatively, obvious over each of these references separately.

Applicants have canceled claims 1 and 9, and in light of the newly added claims, Applicants request reconsideration of this rejection. Respectfully, Applicants direct the Examiner's attention to the claim for domestic priority under 35 U.S.C § 119(e), to U.S. Provisional Applications 60/055,784 (August 15, 1997), 60/064,926 (November 7, 1997), and 60/065,367 (November 12, 1997). The Examiner's consideration of this claim for domestic priority under 35 U.S.C § 119(e) is respectfully requested, because a grant of benefit of this priority would render Futreal *et al.* inapplicable as prior art under 35 U.S.C § 102(b).

Furthermore, the invention, as defined by the specification and the new set of claims, relates to coding sequences of the human BRCA2 gene which are distinguishable over the cited prior art. Neither Futreal *et al.* nor Tavgian *et al.* teach the claimed isolated nucleic acid molecules and cDNA of the instant claims. Specifically, claims 61-83 reflect sequences of human BRCA2 that differ from the GenBank genomic sequence of BRCA2 (Accession No: U43746) at two specific nucleotides in exon 15 and the absence of a 16 nucleotide intronic sequence at the 5'- end of exon 16. Also, the GenBank genomic sequence identifies a different intron/exon border at the 5'-end of exon 5. The sequence of human BRCA2 listed in the Breast Information Consortium (BIC) database differs from the present invention in which nucleotides 5551-5560 are CGTTTGTGT, corresponding to amino acids arginine, leucine and cysteine, whereas the corresponding sequence of the present invention is GTTTGTGTT, corresponding to amino acids valine, cysteine and valine. Furthermore, the BIC database describes the nucleotides at positions 2024, 4553, 4815, 5841, and 5972 as T, T, A, C, and T, respectively, whereas the corresponding nucleotides of the present invention are C, C, G, T, and C, respectively. The nucleotide differences at positions 2024, 4553 and 5972 translate to different amino acid residues at corresponding positions in the BIC BRCA2 polypeptide and the BRCA2 polypeptide of the present invention.

In addition, the present invention relates to polymorphisms at nucleotide positions that correspond to nucleotide positions 1093, 1593, 2908 and/or 9079 as set forth in SEQ ID NO: 4. The specific nucleotide changes at these positions, relative to the nucleotide identity of these nucleotides in the GenBank sequence (Accession No: U43746) are polymorphisms identified in patients that do not have a predisposition for breast or ovarian cancer. (See Figure 3). Applicants respectfully request that this rejection of the claims be withdrawn.

7. Conclusion.

Applicants believe that the differences cited and discussed in detail herein distinguish the claims, as currently presented, over the cited references. Applicants respectfully request withdrawal of the outstanding rejections and early notice of allowance to that effect.

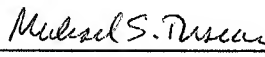
EXCEPT for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

If the Examiner finds that a telephone conference would further prosecution of this application, she is invited to call the undersigned.

Respectfully submitted,

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Dated: September 18 2000



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